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THE EFFECT OF CERTAIN DRUGS UPON THE GALVANIC SKIN RESPONSE.

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THE Galvanic Skin Response (GSR), arising from activity in the autonomic nervous system, can be recorded as a change in potential difference or in apparent resistance between, for example, the palmar and dorsal surfaces of the hand. It is elicited by stimuli ranging from mild disturbances, such as a deep breath or a cough, to major emotional situations. It seems to indicate some aspect of the degree of general arousal or specific reaction of the organism; moreover it can be very useful simply as a response signal from organisms which for some reason cannot or will not answer the more usual types of question (e.g. animals and young children; psychotics; subthreshold perception situations).

In this paper the GSR potential will be referred to as the Electro-Dermal Response of Tarchanoff, EDR (T), to distinguish it clearly from the GSR by the resistance method, i.e. the Electro-Dermal Response of Féré, EDR (F), and from the various other potentials which the skin generates (e.g. the Electro-Dermal Response of Ebbecke, EDR (E); see Rothman (1954) for a comprehensive review of the electrical phenomena of the skin).

The work reported here stems from a larger study on Electro-Oculography (Shackel, 1957*a*) during which it was found necessary to investigate ways of reducing the EDR (T) and other skin potentials which interfere with or occlude the required Electro-Oculographic signals. To approach physiological zero potential at a recording electrode it would seem necessary to convert the skin from a live and active structure into an inert conducting medium. It was thought that the solution might be to produce an area of very local anaesthesia under the conducting electrode itself; a review of the literature confirmed this as a reasonable hypothesis, at least as far as the EDR (T) was concerned. It was

found (Experiment 1) that a local anaesthetic does effectively diminish the EDR (T). Subsequently a simpler way was found of achieving the same result (Shackel, 1957*b*) ; but Experiments 2 and 3 were done to amplify the results of Experiment 1, because the matter seemed interesting by itself apart from the initial problem of improving zero stability with DC recording techniques.

EXPERIMENT 1.—LIDOCAINE + ADRENALIN AND THE EDR (T).

Six volunteer male subjects were used to test the question : Is the EDR (T) from the palm significantly diminished if the skin beneath the surface electrode is locally anaesthetized, and if so to what extent ?

Method.

The EDR (T) potential changes elicited by two types of stimulus, a deep breath held for a few seconds and a bang from a wooden clapper (out of sight behind the subject's head), were recorded from the left palm under the various treatment conditions. Two separate sets of electrodes, and two recording channels, were used, one electrode set always being "normal", that is on untreated skin. Each set comprised one "live" electrode on the palm, one "neutral" electrode on the relatively "inactive" (Floyd and Keele, 1936) upper forearm, and one earth electrode at the wrist to minimize hum pick-up. Thus the two electrode sets enabled comparison of the response from one palmar area with that from the other, both responses being made at the same instant to the same stimulus.

At the first session for all six subjects both palmar areas were untreated ; this was to check that substantially similar response amplitudes came from both, by comparison with any subsequent differences caused by treatments, and to pick out for treatment which of the two gave the larger response, thus ensuring that any bias should be against showing treatment differences. At the subsequent sessions two subjects continued without treatment as controls, and the other two pairs received anaesthetic and saline injections in reverse order. The control subjects received an anaesthetic injection at the end of the final session to confirm the treatment effect with them also. The experimental sequence was thus :

Subject.		Session 1.		Session 2.		Session 3.
1, 2	. .	Control	.	Saline	.	Anaesthetic.
3, 4	. .	Control	.	Anaesthetic	.	Saline.
5, 6	. .	Control ₁	.	Control ₂	.	Control ₃ then anaesthetic.

A satisfactory anaesthetic injection was of course conveniently signalled, both in extent and duration, by the resulting white, vasoconstricted area caused by the adrenalin. The compound and quantity used was adequate to

anaesthetize an area at least $\frac{3}{4}$ in. in diameter for at least half an hour. The limits of the anaesthetized area were always checked also by stroking and scratching with a needle point so that the electrode could be correctly positioned on it.

The saline injection was a control treatment, lest any result should be a function merely of piercing the upper layers of the skin and injecting the physiological saline which is the vehicle for the anaesthetic. The electrode was always placed over the needle puncture in the saline treatment sessions; it was not necessarily placed over the needle puncture in the anaesthetic sessions. Each day the electrodes were replaced on the same skin area within a one inch diameter circle.

The anaesthetic compound was 1% lidocaine, with 1/100,000 adrenalin, in a Ringer's solution (1% Xylotox E.100). The saline solution was 1% sodium chloride in distilled water. 0.5 c.cm. of the appropriate solution was administered by intradermal injection at the beginning of the treatment session. The subjects inevitably knew the difference between treatments, but they were not told what results were expected until the end of the whole test; even had they known it seems unlikely that they could have influenced the results.

As soon as the injections had been given the subject was seated, the two electrode sets were attached, and at least ten stimuli of each type were given in a mixed, though not randomized, order. The gain of each recording channel was kept as high as possible, consonant with keeping the EDR (T) signal within the limits of the pen recorder chart, to ensure easy and accurate scoring; each record was separately calibrated. The EDR (T) readings given in the tables below are therefore certainly accurate to the last decimal place. At the end of each session one or two extra responses of each type were recorded with identical gain in both channels; a typical example is shown in Fig. 1.

Apparatus.

The electrodes were a rubber suction cup type, of effective surface contact over an area $\frac{3}{8}$ in. in diameter, similar to those described by Andrews (1939). A type developed from these (Shackel, 1957c) was used for the later experiments. When recording DC potentials of the relatively small amplitude detected in these tests, it has been found necessary to take considerable care in preparing the silver silver-chloride electrodes and 1% sodium chloride jelly if zero drifts are to be avoided; with suitable preparation an average short term stability (i.e. for 10 seconds, longer than the duration of any one EDR (T) signal) of 10 microvolts can be achieved.

The recording system was a two-channel DC amplifier (Shackel, Sloan and Warr, 1957) and pen recorder; the smallest change in signal level reliably recorded is less than 10 microvolts.

Results.

The individual means and standard deviations of the EDR (T) scores for the four subjects in the various treatment conditions are quite compatible and so are not given separately. Their combined results are given in the first part of Table I. There is no need to assess statistically the significance of the difference between comparative results from normal untreated (N.) and anaesthetized (Anaesth.) skin, clearly the data came from two completely separate populations. A similar but saline injection obviously does not have an effect large enough to

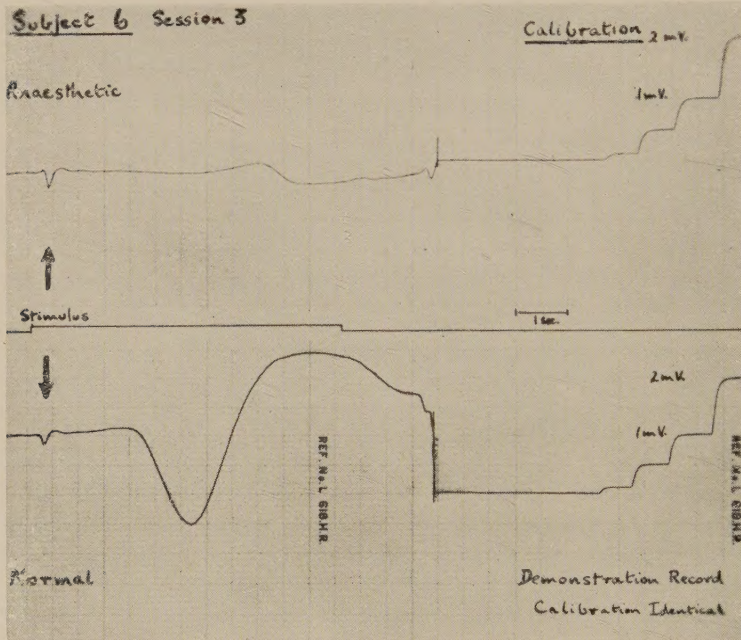


FIG. 1.—A typical record of EDR (T) from normal and anaesthetized palmar skin.

explain the difference in the data, and therefore we may conclude that the anaesthetic compound does significantly diminish the EDR (T).

The individual scores for the separate sessions of the two control subjects are given in the second part of Table I. These show that two adjacent palmar areas, although not necessarily giving identical scores, certainly do not differ enough to invalidate the conclusion drawn from the treatment results; the anaesthetic injection at the end of the third session confirms the treatment effect on these subjects also.

The grand averages of the comparable scores from the normal and anaesthetized skin areas of all six subjects are given in the third part of Table I. On an average the anaesthetic reduces the EDR (T) to about $1/13$ of its normal level; the reduction ratio for individual subjects varies from 8 : 1 to 25 : 1.

TABLE I.

(All Readings in millivolts.)

EDR (T) Results from Treatments (Subjects 1, 2, 3, 4).

		Deep breath stimulus.				Noise stimulus.			
		N. Saline.		N. Anaesth.		N. Saline.		N. Anaesth.	
Mean	.	1.3	0.9	1.4	0.08	1.7	1.2	1.6	0.09
S.D.	.	0.6	0.45	0.6	0.05	0.75	0.7	0.6	0.05

(Each mean = average of at least 40 readings.)

Individual EDR (T) Results from Controls (Subjects 5, 6).

		Deep breath stimulus.				Noise stimulus.			
		Control ₁ .		Control ₂ .		Control ₃ .		Anaesth.	
		N. N.	N. N.	N. N.	N. N.	N. N.	N. N.	N. N.	N. N.
5. Mean	.	3.0	3.2	1.8	1.7	0.9	0.9	1.1	0.14
S.D.	.	1.5	1.7	1.1	0.9	0.3	0.4	0.5	0.07
6. Mean	.	3.0	3.5	1.7	1.1	1.7	1.4	1.2	0.10
S.D.	.	2.6	3.0	0.7	0.6	0.8	0.9	0.6	0.05

(Each mean = average of at least 10 readings.)

Effect of Anaesthetic on EDR (T).

		Deep breath stimulus.		Noise stimulus.	
		N.	Anaesth.	N.	Anaesth.
Mean	.	1.3	0.10	1.5	0.11
Ratio N : Anaesth.	.	13 : 1		14 : 1	

(Each mean = average of at least 60 readings.)

EXPERIMENT 2.—LIDOCAINE AND THE EDR (T).

Experiments 2 and 3 were conducted to investigate the relative potency of lidocaine and adrenalin, the two main constituents of the anaesthetic compound, in diminishing the EDR (T). This was thought particularly desirable since Darrow (1937, 1936) reported that intravenous injections of 1/1000 adrenalin caused a "marked reduction" or "suppressed" the EDR (F).

Four subjects were used to test the question: Is the effect on the EDR (T) of lidocaine alone different from the effect of lidocaine + adrenalin, and if so to what extent?

Method.

It was decided to compare the response to the two types of injection on successive days on the same subjects; it was thought that to inject two areas on the palm with the two different substances at the same time might confound the results.

Because the control sessions of Experiment 1 had shown that the EDR (T) from adjacent palmar areas was substantially the same (with the largest ratio

difference 1.6 : 1 and the average 1.18 : 1) a similar control session was not repeated ; instead the choice of which area of the inner aspect of the palm, that nearer the wrist or that nearer the fingers, should be used first for treatment, was included as part of the balanced design. The untreated area for the "normal" electrode was the same for both sessions, a point towards the centre of the palm about equidistant from both the treatment areas. The two pairs of subjects received the two treatments in reverse order :

Subject.	Day 1.	Day 2.
1, 2 .	Lidocaine + Adrenalin .	Lidocaine only.
3, 4 .	Lidocaine only .	Lidocaine + Adrenalin

The lidocaine + adrenalin compound was identical with that used in Experiment 1 ; the lidocaine only compound was identical with this except for the absence of adrenalin (1% Xylotox SE) ; 0.4 c.cm. of the appropriate compound was administered in the same way as before. Extra care was taken to check the boundaries of the area anaesthetized with lidocaine only and to place the electrode precisely, because of course no visual indication was available as a guide.

In all other respects the general procedure was the same as in Experiment 1.

Results.

The combined mean EDR (T) scores from all four subjects for the two types of injection are given in Table II :

TABLE II.					
(All readings in millivolts.)					
<i>Lidocaine + Adrenalin.</i>					
			Deep breath stimulus.	Noise stimulus.	
			N. L. + A.	N. L. + A.	
Mean	2.8	0.34		2.5	0.27
Ratio N : L. + A.	8 : 1			9 : 1	
<i>Lidocaine Only.</i>					
			N. L.	N. L.	
Mean	2.1	0.41		2.3	0.39
Ratio N : L.	5 : 1			6 : 1	
(Each mean = average of at least 40 readings.)					

EXPERIMENT 3.—ADRENALIN AND THE EDR (T).

Five subjects were used to test the question : Is the effect on the EDR (T) of adrenalin alone different from the effect of lidocaine + adrenalin, and if so to what extent ?

Method.

For administrative reasons this test had to be run separately instead of in a combined design with Experiment 2. Because the data from Experiments 1 and 2 on the effect of lidocaine + adrenalin on the EDR (T) are substantially similar, it was considered unnecessary to repeat the comparison type of test sequence of Experiment 2. Instead a "before and after" test was made on the same skin areas in one experimental session.

Electrodes were placed exactly as for the first "control" session of Experiment 1; the usual stimuli were given; then the electrode of whichever palmar area was giving the larger response was removed and that area was injected with 0.4 c.cm. 1/100,000 adrenalin. The electrode was replaced and the stimuli were repeated. Good vasoconstriction as indicated by whitening of the skin was noted in all cases.

Results.

The averages of the scores from all subjects are given in Table III. As was expected, the average level of response is shown by the untreated skin area (N_1) to be the same in both the control and the treatment parts of the test. It is therefore reasonable to compare directly the responses before and after treatment from the treated skin area ($N_2 : A$) in order to assess the effect of the adrenalin injection.

TABLE III.

(All readings in millivolts.)

Same Skin Areas Before and After Adrenalin Injection.

	Deep breath stimulus.				Noise stimulus.			
	Control.		Adrenalin.		Control.		Adrenalin.	
	N_1 .	N_2 .	N_1 .	A.	N_1 .	N_2 .	N_1 .	A.
Mean . . .	1.1	1.5	1.1	0.77	1.5	2.2	1.5	1.1
Ratio $N_2 : A$. .	1.9 : 1				2 : 1			

(Each mean = average of at least 40 readings.)

DISCUSSION.

From a review of the literature it seems well established that the EDR (T) and the EDR (F) are closely related phenomena and that they probably arise from the same general source (Darrow, 1927; Jeffress, 1928); it seems fairly certain that they are both subserved by some aspect of sweat gland activity (McCleary, 1950; Wagner, 1952). It also seems well established that atropine effectively diminishes most forms of eccrine sweat secretion (e.g. Chalmers and Keele, 1951; Rothman, 1954). However, detailed quantitative results of the

effect of atropine and other drugs on the EDR (T) or the EDR (F) seemed scarce ; the main evidence which has been found is summarized below.

The Administration of Atropine.

(a) Increases palmar resistance : Richter (1929), 1/50 grain subcutaneously in upper arm, 40 human subjects ; increase in all cases " in some great, in others slight but still definite " ; only one " typical " result quoted—increase from 25 Kilohms to 280 Kilohms after 1½ hours—no other quantitative data given.

(b) Decreases EDR (F) : Farmer and Chambers (1925) refer to Leva and to Herman and Lucksinger, who reported that atropine caused the response to disappear. Waller (1919) quotes Leva at length, and the results are clearly not quantitative. On the other hand Waller (1919) and Aveling and McDowall (1926) reported that the response was undiminished by atropine, but again no quantitative results are given.

(c) Decreases EDR (T) in cat : Patton (1949), 0.1 mg. per kg., intravenously in upper leg, 5 cats ; electrical recording of toepad response to shock stimulation applied to lumbar sympathetic chain ; " complete and irreversible sudomotor paralysis consistently produced " but results given from only one " typical " experiment ; graph is plotted of drop in EDR (T) to zero after 5 minutes, but uncalibrated photographic recording, showing a large drop in response, shows some response still occurring (perhaps 100 to 200 μ V., by guessing a likely calibration) ; the result is unquestionably clear and highly significant, but full quantitative data are not given.

The Administration of Adrenalin.

(a) Increases palmar resistance : Richter (1929), 1 c.cm. 1/1000 suprarenalin subcutaneously in upper arm, 40 human subjects ; " in almost every subject a slight increase occurred, but there were marked individual differences in the magnitude of this increase " ; no quantitative data given. O'Leary (1932), 1 c.cm. 1/10,000 adrenalin chloride subcutaneously (not stated where), numbers uncertain but probably 1 anaesthetized cat ; no effective change in either paw (one normal, one sympathetomized) ; same injection intravenously (not stated where), number uncertain but probably 1 or 2 anaesthetized cats ; sympathetomized paw again steady, normal paw increased from 620 ohms to 980 ohms after 5 minutes and still 870 ohms after 25 minutes.

(b) Decreases " spontaneous " (" emotional ") sweating : Sonnenschein *et al.* (1951), incidental observation during experiment on the direct sweating response elicited by adrenalin ; 0.05 to 0.1 c.cm. 1/1000 or 1/100,000, intradermally in forearm, 17 human subjects : inhibition of spontaneous sweating appeared within a few minutes to 2 hours after the end of the direct sweating response and lasted for one hour up to 24 hours or longer ; iodine-starch paper recording method used, but no quantitative data given of relative sweat dot counts before and after injection.

(c) Decreases palmar EDR (F) : Densham and Wells (1927), 1/10,000 adrenalin chloride by electrophoresis for 5 to 10 minutes into two fingers of right hand, 2 subjects ; EDR (F) measured from fingers, with the solution as a recording electrode, and expressed as a percentage of the basic skin resistance ; response reduced from 10% and 7.9% to 4% and 4.8% respectively, i.e. was about halved after administration of adrenalin. Darrow (1937) states : " Dr. R. L. Jenkins and I have observed a marked reduction in palmar galvanic reactions to sensory stimulation following intravenous injection of as little as 0.05 c.cm. of 1/1000 adrenalin " but gives no other data.

From this review of the literature it was inferred that both atropine and adrenalin might be expected to have some effect on the EDR (T), but it seemed clear

that an experiment was needed. An alternative to atropine was thought desirable because possible side effects were a contra-indication to its use in the original application envisaged. Dale and Feldberg (1934) showed that acetylcholine is the chemical transmitter between the endings of the sweat nerve fibres and the sweat glands. Dawes (1946) refers to various workers who have shown that procaine, among other substances, antagonizes the effect of acetylcholine on many different types of tissue, this inhibition effect being similar to that of atropine. Rothman (1954) describes the work of Keller showing that "tonus potentials" of the skin, presumably related to the basic level of skin resistance, are diminished by atropine and that "potentials decreased by atropinization could be further decreased by procainization". Lidocaine has been shown (Wiedling, 1952; Goodman and Gilman, 1955) to be more effective than procaine but with a similar general type of action. Lidocaine with adrenalin was therefore used in Experiment 1, and the effect of the separate constituents was studied in the subsequent experiments.

It may be concluded that lidocaine with adrenalin, lidocaine alone and adrenalin alone, in the form and manner used in these experiments, reduce the EDR (T), and presumably also the related sweat gland activity, on average to about $\frac{1}{10}$, $\frac{1}{5}$ and $\frac{1}{2}$ respectively. It is generally accepted (Goodman and Gilman, 1955) that the action of local anaesthetic compounds is enhanced and prolonged by the added adrenalin, because the vasoconstriction thus induced delays absorption and dissipation of the anaesthetic. Whether this is also the reason for the greater reduction of the EDR (T) by lidocaine with adrenalin, or whether these two substances are acting in different ways, or on different structures, and in a truly additive fashion when combined, as might be suggested by their apparently proportionate effects in the experiments reported here, is an interesting problem requiring further experiment.

It would be interesting to know how lidocaine takes effect on the EDR (T): by diminishing the conduction rate of the sympathetic nerve fibres; by inhibiting the action of the acetylcholine release mechanism at the nerve ending; by diminishing the sensitivity of the sweat gland to acetylcholine; or perhaps in more than one way simultaneously. The last seems the more likely possibility as far as procaine is concerned (Dawes, 1946 (discussion); Goodman and Gilman, 1955, pp. 357-9).

It would be interesting also to be able to compare the relative effectiveness of atropine and of lidocaine with adrenalin in diminishing the EDR (T), but no detailed quantitative data of the type presented here have been found in the literature about atropine. Even Patton (1949), who draws attention to his use of a quantitative and objective recording technique, reports "complete sudomotor paralysis" but gives the data from only one typical recording.

The apparent relative ineffectiveness of adrenalin in diminishing the EDR (T), as reported here, seems a little surprising in view of Darrow's (1937)

report of "marked reduction" in palmar EDR (F). Perhaps the difference may be explained by the fact that Darrow's injections were intravenous; the slender evidence of O'Leary (1932) might be taken to support this explanation. But Sonnenschein *et al.* (1951) with intradermal injections also report inhibition of spontaneous sweating at the site of the injection in the forearm; perhaps adrenalin may be a less effective inhibitor in the palm because of some significant difference between the two areas in the structure or mode of operation of the sweat gland system. Certainly Densham and Wells (1927) with meagre but quantitative data, report a reduction of only about 50% in the EDR (F) on the finger, a result very similar to that of Experiment 3. Thus the reported evidence on this aspect of the autonomic effect of adrenalin seems contradictory and in need of further study.

The difficulties and contradictions of some of the results from studies of sweating, skin resistance and Galvanic Skin Responses may well be resolved if there indeed exist differing modes of operation of the eccrine sweat gland system in different areas, or if there are two separate, and to a certain extent independent, response mechanisms at work. This latter possibility has been suggested by Forbes (1936) as the basis for the two types of signal which he showed to occur within a single Galvanic Skin Response, and which he termed the *a* and the *b* response respectively. It is thought that this possibility might well be investigated by using the comparative recording method of this paper to see whether any drugs show a selective effect on the *a* or the *b* response.

From the review of the literature it was surprising to find that there seemed to be a shortage of exact quantitative results on the particular aspects of the Galvanic Skin Response discussed here. These experiments are therefore reported, although they seem to raise more questions than they answer, because it is thought that they provide some quantitative data which bear directly upon any theory of the nervous and chemical mechanisms subserving the EDR (T) in particular and probably eccrine sweat gland activity in general.

SUMMARY.

The effect of certain drugs, injected intradermally, upon the palmar "emotional" GSR potential has been studied and is reported with quantitative results. Lidocaine with adrenalin, lidocaine alone, and adrenalin alone, have been found to reduce the GSR potential respectively to about $\frac{1}{10}$, $\frac{1}{5}$ and $\frac{1}{2}$ of its normal value. The implications of these results for studies of the mechanisms subserving the Galvanic Skin Response are tentatively discussed.

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CHOLINERGIC "URTICARIA" AND MILIARIA.

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PSYCHOGENIC URTICARIA was known to some of the earliest writers on urticaria, and Bateman (1829) remarks that "the eruption occurs chiefly in summer, and affects persons of full habit who indulge in the gratifications of the table, or suffer from domestic afflictions and other causes of anxiety". Nervous causes for urticaria are referred to by Török (1928) and a clearly defined pattern of nervous urticaria was called "cholinergic urticaria" by Grant, Pearson and Comeau (1936). This disease is manifested by urticaria-like attacks, regularly induced by emotion, exercise or warmth, and characterized by numerous flares around minute wheals accompanied by itching. The lesions last about one hour, and Grant *et al.* believe that they correspond closely with the normal skin reaction to the introduction intracutaneously of histamine solution. Evidence will be produced in favour of the view that the eruption called cholinergic urticaria is not a simple dermal oedema, but is an epidermal lesion associated with sweat ducts.

Grant and his colleagues showed that, in patients with this disorder, reflex heating of the skin brought about by warming the lower limbs produced the eruption on the unimmersed parts of the body. A sphygmomanometer cuff applied so as to occlude the arterial circulation to an arm before heating as described prevented the appearance of the eruption on the occluded arm; but on removal of the cuff an intense eruption appeared on the arm at a time when the generalized rash on the body was subsiding. This suggests that during arterial vascular occlusion changes were brought about which caused the eruption to appear as soon as the circulation was restored. Blocking of a cutaneous nerve by a local anaesthetic prevented the development of the eruption on the anaesthetized patch of skin. This is unlike the findings in a histamine wheal. Carbachol and pilocarpine administered subcutaneously produced the eruption. Atropine sulphate was capable of preventing the rash on heating the lower limbs.

From these experiments, Grant *et al.* concluded that the lesions in these patients were due to the liberation of acetylcholine from nerve endings, which resulted in the liberation of "H-substance" and subsequent wheal formation. They were not certain of the pathways involved, but found no evidence that the sweat apparatus was involved. They noted that if collodion was applied to the skin before heating commenced, much more intense whealing occurred beneath the collodion, and attributed this to a slowing of the blood-flow beneath

the membrane due to tension, and consequent accumulation of H-substance in greater concentration.

Marchionini and Ottenstein (1931) found that a sweat bath and pilocarpine injections were effective in producing the eruption in such patients, and they considered a sensitivity to sweat to be the main cause of the disease.

Grant *et al.* were not able to demonstrate sensitivity to sweat obtained from the patient's own skin or to sweat from normal patients. The sweat from cases of cholinergic urticaria did not differ in pH value, or in quantity produced, from that of normal controls.

Herxheimer (1956) suggests that there is strong evidence that the skin changes in cholinergic urticaria are mediated by fibres of the sympathetic system and that, contrary to the conclusions of Grant *et al.*, there is an intermediate link between the release of acetylcholine from the nerve endings, and the appearance of skin lesions; and that this link is some product of sweat-gland activity. Herxheimer has shown, by sweat prints after unilateral cervical sympathetic block, that there is less sweating and fewer lesions on the side of the sympathetic block after heating than on the control side. After generalized ganglionic blocking by hexamethonium bromide, fewer lesions (and decreased sweating) followed exercise compared with the eruption occurring on exercise before the administration of hexamethonium bromide.

These sympathetic block experiments show that the eruption is mediated by sympathetic nerves. The only sympathetic fibres to the skin that are definitely cholinergic are those innervating sweat glands. No drugs or external stimuli were found to produce sweating or vasodilatation separately. Despite various experiments, Herxheimer was unable to prove whether cholinergic urticaria was associated with sweating or with vasodilatation, but was of the opinion that it was always associated with both.

Sulzberger and Herrmann (1954) speculated that some cases of cholinergic urticaria might fall in the category of sweat-retention urticaria.

INVESTIGATION.

Two patients suffering from typical attacks of cholinergic urticaria have been studied in this department. Both were young men in their thirties who described attacks of small irritating wheals which occurred at embarrassing interviews, at dances, or when playing football. Hot weather always made the disease worse.

Whealing could be produced in both patients by warming the arms in water at 45° C. for 20 minutes, or by an injection of pilocarpine, or by exercise on a stationary bicycle. One patient complained that he could not sweat and, whenever he got hot, the rash appeared. In both patients, during whealing produced by heating, copious sweating occurred from axillae, neck, face,

groins and feet, but only a little sweating on trunk and thighs where lesions appeared most profusely.

The wheals consisted of papules 2-3 mm. in diameter, dome-shaped and pale pink, and around them an intense flare spread over an area $1\frac{1}{2}$ inches in diameter. There were no pseudopodia. Lesions were produced experimentally by heating the arms in water at 45°C . and were excised as biopsy specimens. The histological findings were as follows :

Case 1.

One sweat duct showed intercellular oedema and partial disruption of the lining cells in the superficial part of the duct at the point where it passed into



FIG. 1.

the epidermis (Fig. 1). There was some fluid exudation into the dermis at this site. Although the duct opening showed a keratotic ring, no proof of poral closure could be demonstrated in serial sections.

Case 2.

The sweat duct was tortuous and the lining cells at the superficial end were separated by oedema. In the epidermis there was a vesicle which was in close apposition to the sweat duct (Fig. 2). There was no evidence of poral closure in this section.

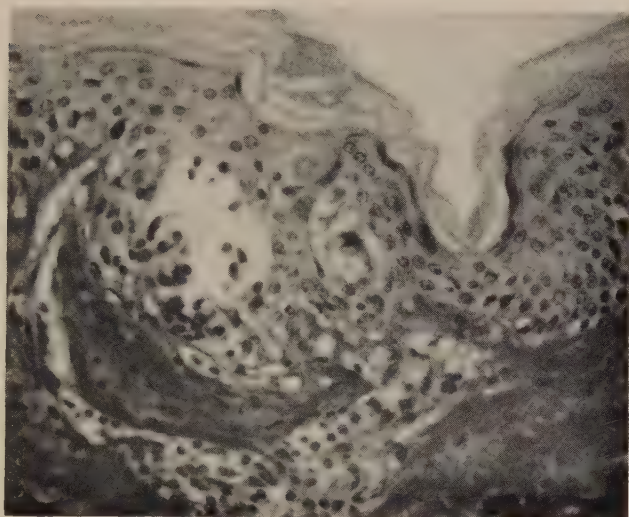


FIG. 2.

DISCUSSION.

These findings suggest that the lesion that has been called cholinergic urticaria is not primarily a dermal oedema, but is a spongiotic epidermal lesion having many features in common with the changes described by O'Brien (1947) in prickly heat. The main factors in the causation of this disease are reviewed by Goldsmith and Hellier (1954). According to O'Brien, poral closure is a constant feature of the condition and gives a mechanical explanation for the histological findings which suggest trapped sweat. More recently Hambrick and Blank (1956) have thrown doubt on the theory that keratotic plugging is responsible for sweat retention.

Assuming the lesions demonstrated in my cases to be comparable with miliaria, the views of Hambrick and Blank would be supported by the failure to find duct occlusion.

The importance of serial sections is stressed in the study of sweat-gland pathology, since it is realized that slightly oblique sections across the mouth of a duct would include some of the opposite wall of the duct. This would be superimposed on the duct opening and give a false impression of plugging.

Lesions resembling urticarial wheals could conceivably occur in cholinergic urticaria if exudation of sweat from the disordered sweat duct occurred mainly from the subepidermal portion of the duct.

O'Brien recommended the use of lanolin for miliaria, on the grounds that softening the keratin plugs will allow the free drainage of sweat ducts. Accordingly my patients were given lanolin to apply twice daily, but no benefit resulted. Ultra-violet ray treatment was then given in mild exfoliating doses

twice weekly for two months. After this the patients have been symptom-free for twenty months and six months respectively.

CONCLUSIONS.

The small pale papule surrounded by a large flare is not typical of urticaria of the histamine type.

The structural changes in the epidermis demonstrated in two cases confirm the views of Herxheimer that the sweat apparatus is involved in cholinergic urticaria. The histological appearances are comparable with those of miliaria.

The increased whealing under collodion painted on the skin would be expected if the disease were analogous to prickly heat, which is accentuated by maceration, and adherent substances such as adhesive zinc oxide plaster and collodion.

Treatment with lanolin was not successful, but exfoliating doses of ultra-violet rays have been effective in both cases here described. The mechanism is not certain.

I am grateful to Dr. W. N. Goldsmith for suggesting the study of these cases ; I also thank Dr. P. J. Hare and Dr. A. Jarrett for their help.

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RELAXIN : ITS EFFECTS IN A CASE OF ACROSCLEROSIS.

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RELAXIN was recognized as an ovarian hormone by Hisaw (1926) ; he noticed that this extract of the corpus luteum produced growth and relaxation of the pelvic ligaments of the guinea-pig. It is a non-steroid hormone, and according to Frieden and Hisaw (1953) is a polypeptide with a molecular weight of less than 10,000.

Relaxin usually appears only during pregnancy in the majority of mammals, but small amounts may be found in the ovaries of non-pregnant sows (Albert *et al.*, 1947). During pregnancy it is found in the serum, ovaries, uterus and placenta. In the human female relaxin is found in the serum at the seventh to tenth week of pregnancy, and increases regularly during the last two trimesters, reaching a maximum concentration at the thirty-eighth to the forty-second week (Perkoff *et al.*, 1954). It is said to disappear from the serum within twenty-four hours after delivery, and is found only in traces in the human placenta.

The action of relaxin is accentuated by oestrogens (Hall, 1948). First there is dilatation of blood vessels in the connective tissue of the symphysis pubis and pelvic ligaments, then oedema of the ground substance and dissolution and splitting of collagen. Similar changes occur in the fibrous portion of the parturient human cervix (Folsome *et al.*, 1956).

Relaxin can only be administered parenterally, and is rapidly excreted in the urine in an inactivated form (Zarrow and Money, 1948). Perkoff *et al.* (1954) claim to have first studied the effects of relaxin in human subjects. They noted that the relaxin activity of one injection lasted only six hours, but were able to produce "physiological" levels in the serum without adverse effects ; there was no change in the blood pressure, pulse rate, leucocyte count, differential leucocyte count and the total eosinophil count. The plasma hydroxycorticosteroids and excretion of 17-ketosteroids in the urine were unaltered. The serum electrolytes, urea, alkali reserve and glucose were unaltered ; the plasma volume remained unchanged. The only biochemical change noted was a rise in the daily excretion of creatine in the urine after several days of therapy.

Subsequent investigators have confirmed the safety of relaxin, which has been used therapeutically mainly in midwifery for the treatment of premature labour, uterine inertia and cervical dystocia (Abramson and Reid, 1955 ; Eichner *et al.*, 1956 ; Folsome *et al.*, 1956). Unpublished reports have suggested

that relaxin, because of its action on ground substance and collagen, may be of some use in the treatment of scleroderma.

CASE REPORT.

A married woman aged 63 years.

The scleroderma began in 1946 and gradually became widespread, and she became almost entirely bedridden. Her skin became thickened and inelastic, and in areas atrophied. The areas most affected were the face, neck, hands and legs. Her face exhibited the characteristic mask of atherosclerosis, with pinched nose, taut wrinkled mouth, and telangiectases. Earlier in her illness she suffered from Raynaud's phenomena, and now had sclerodactyly. There were flexion deformities of both knee-joints and limitation of flexion and rotatory movements of the neck. She was unable to sit up unaided. She felt encased, and there was muscle wasting and weakness.

There was evidence of visceral involvement. A prominent symptom was dysphagia which had begun five years previously and now she was unable to swallow solids. The radiologist reported (21 : v : 57) rigidity of the oesophagus, loss of peristalsis, stricture of the lower end and dilatation above this. There was also a hiatus hernia. She also complained of spasms of central abdominal pain, and during a barium meal examination traces of barium were seen in the small intestine after ten hours ; this was taken as indicating some involvement of the small intestine.

Other skiagrams showed bilateral pulmonary fibrosis and cardiac enlargement, and osteoporosis of the hands and legs. She also had left bundle branch block which had developed since the onset of her illness.

Blood count : Hb 7.8 g. ESR, 60.

Thymol turbidity, 5 units ; thymol flocculation, ++ + + ; zinc sulphate turbidity, 12 units.

A low urinary excretion of 17-ketosteroids (1.5 mg. in 24 hours) could have been due only to her age, to her poor nutritional state or may have indicated involvement of the gonads or the adrenals. The serum electrolytes were normal. Two skin biopsies confirmed the diagnosis of scleroderma.

Previous treatment with carbacol ionization, oral and parenteral prostigmine, papaverine hydrochloride and priscol had produced no improvement. Some relief of symptoms and a short remission had been produced, however, with hydroxyphenyl cinchoninic acid.

Treatment.—A brand of relaxin known as Releasin was used, which was manufactured in the Warner-Chilcott laboratories in New York, U.S.A., from the ovaries of pregnant sows. Releasin is water-soluble, and 1 ml. contains the equivalent of 20 mg. or 3000 guinea-pig units of relaxin standard. (One G.P.U. is the amount of relaxin which will induce an unmistakable relaxation of the symphysis pubis in two-thirds of a group of twelve castrated guinea-pigs weighing between 350–380 g.). Because the action of relaxin is enhanced by priming with oestrogens, stilboestrol in doses of 2 mg. daily was given for fourteen days (10 : v : 57 to 24 : v : 57). This was followed immediately by Releasin, 1 ml. intramuscularly daily for one week (24 : v : 57 to 30 : v : 57). Because of an improvement in symptoms the dose of Releasin was increased to 2 ml. daily for a further period of fifteen days (31 : v : 57 to 14 : vi : 57). The injections were not associated with any allergic reactions, but produced slight pain for five to ten minutes at the site of injection.

The first sign of improvement, namely ability to flex the fingers, appeared within twenty-four hours of the beginning of treatment. At the end of the first week improvement was quite marked, and she was able to move her head and could sit up unaided. She was now free from abdominal pain. By the time she had completed the course of treatment she could swallow solids, although the barium bolus showed no change

in the appearance of the oesophagus (11 : vi : 57). On 2 : viii : 57 the radiologist reported that the oesophagus was less rigid and the barium passed through it more quickly. On 1 : xi : 57 he reported further improvement in that the passage of the bolus was quicker, the narrowing at the lower end was less and the hiatus hernia was smaller. At the end of the course of treatment she also lost the sensation of general restriction—something which she had not been free from for a number of years. So far, improvement has been maintained for five months after the cessation of treatment.

During treatment there was no alteration in the pulse rate, temperature or blood pressure. Her haemoglobin rose to 10.9 g.%, and the ESR fell to 49. The serum electrolytes were unaffected and the 17-ketosteroid excretion in the urine was not significantly affected. The excretion of creatine rose from 70 mg. to 140 mg. in twenty-four hours. There were no allergic reactions.

A further skin biopsy was not taken during treatment, and it was not possible to estimate serum relaxin during therapy.

DISCUSSION.

Scleroderma is, in part, a disease of collagen (Klemperer *et al.*, 1942 ; Goetz, 1945). The basic lesions in the skin are an increase in connective tissue and vascular changes, namely medial arterial proliferation and round-cell infiltration of the adventitia. Similar changes occur in the viscera, plus oedema, cellular infiltration and eventually atrophy of parenchyma. (Matsui, 1924 ; Goetz, 1945 ; Shuford *et al.*, 1953.) Therefore relaxin, which has a profound effect on connective tissue, might be expected to produce some relief of this condition. Releasin had this effect in this patient, and produced rapid and progressive relief.

Patients with acrosclerosis may feel improved as a result of treatment when it is difficult to confirm this objectively, and in some cases spontaneous remissions may occur. A variety of unrelated drugs used on a more empirical basis than relaxin have produced remissions. Because of this, it is difficult to assess the effects of treatment. In this patient a response within twenty-four hours of beginning treatment and the maintenance of improvement long after the patient's serum could have retained any relaxin activity may lead one to suspect that an element of suggestion crept in. However, allowing for the possibility of this there was an appreciable improvement, and the relief of the dysphagia was striking and was confirmed radiologically.

It is commonly accepted that the main lesion in the oesophagus in this condition is atrophy of the muscle with minimal connective tissue replacement (Abrams *et al.*, 1954). However, dense collagenous changes in the submucosa were previously described by Goetz (1945) and Lusbaugh *et al.*, (1948). It is probable that both types of change occur, and therefore relaxin might be expected to produce some relief. The radiological appearances suggest that both processes are at work. Usually there is reduction in peristaltic activity in the lower segment of the oesophagus, with dilatation and rigidity. Later some cases develop stenosis above the phrenic ampulla and a hiatus hernia. Shanks and

Kerley (1950) suggested that these latter changes were due to impairment of the cardiac sphincter due to sclerodermatous infiltration allowing regurgitation of stomach contents which would produce the sequence of oesophagitis, ulceration and later contraction which would cause a hiatus hernia. Earlier Buckstein (1948) had suggested that acrosclerosis produced stenosis of the lower end of the oesophagus, and by cicatricial shortening would pull up a hiatus hernia. Johnstone (1952) later saw similar changes radiologically in the oesophagus when at autopsy there was no evidence of stenosis, and suggested that the apparent stenosis was due to spasm of vagal origin. However, it seems that more often an organic stenosis occurs, although spasm may play some part in early cases. Certainly spasm did not seem to be the explanation in the case reported above, as the constriction appeared in the same site at each radiological examination.

As relaxin is produced from the ovaries of pregnant sows, it is a relatively scarce hormone and could not be used as a prolonged treatment in the doses given in this patient. There may be some place, however, for giving short courses in cases of scleroderma in the hope of producing remissions and allaying severe complications such as dysphagia. As with other forms of therapy used in acrosclerosis, it seems that relaxin does not affect the fundamental cause of this disease, whatever that might be, and unpublished reports indicate that, as might be expected, symptoms gradually return after cessation of treatment.

SUMMARY.

A case of acrosclerosis was treated with a short course of relaxin preceded by a course of oestrogens.

A partial remission was produced, with marked relief of symptoms, especially dysphagia.

There were no allergic or systemic reactions to the injection of this hormone. The excretion of creatine in the urine rose towards the end of treatment.

I am grateful to Drs. R. Mowbray, J. E. Ennis and G. T. Holroyd for permission to publish details about this case. I am indebted to Wm. Warner and Co., Ltd., for information concerning the use of relaxin in the treatment of scleroderma, and for unpublished reports.

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PLAQUENIL IN THE TREATMENT OF CUTANEOUS LUPUS ERYTHEMATOSUS.

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THIS is a preliminary report on the use of hydroxychloroquine (Plaquenil) in the treatment of cutaneous lupus erythematosus. The therapeutic effects of Plaquenil have been recorded by a number of authors in the United States of America (Mullins *et al.*, 1956; Lewis and Frumess, 1956; Cornbleet, 1956; Bennett and Rees, 1956; Rein and Fleischmajer, 1956) and the opportunity to use the drug prior to its becoming generally available in this country has made possible the following report.

Up to this time the safest and most effective treatment in cutaneous lupus erythematosus has been by means of oral chloroquine (Christiansen, 1956; Lewis, 1955). Side-effects, however, are relatively common and those reported include anorexia, dyspepsia and diarrhoea; visual disturbances with difficulty in accommodation and flickering before the eyes; vertigo and tinnitus; pruritus; nervous disturbances; malaise; urticaria; leucopenia and agranulocytosis; dermatitis; bleaching of the scalp hair, eyebrows and eyelashes (Alving *et al.*, 1948; Christiansen, 1956). On account of these side-effects it is impossible to increase the dose to the therapeutic level in certain cases.

MATERIAL.

Owing to the shortage of Plaquenil only ten patients could be included in this trial, seven of them women and three men. Their ages ranged from 26 to 47. All had typical discoid lupus erythematosus of the face of a severe degree and in four cases this had been confirmed by histological examination. As the main object of the trial was to compare the effect of Plaquenil with that of chloroquine this series included nine patients who had received previous treatment with chloroquine but had proved intolerant of this owing to side-effects. Eight of the nine had suffered from lupus erythematosus for over five years and five for more than ten years.

DOSAGE.

Treatment was started with 200 mg. of Plaquenil twice daily and the dosage was increased at fortnightly or monthly intervals until a satisfactory clinical response was obtained or, as in one patient (Case No. 5), until side-effects occurred. The maximum dosage reached was 2000 mg. daily. In each case treatment was continued for about six months.

RESULTS.

The results are summarised in Table I. It is not easy to assess the improvement in patients with lupus erythematosus but some attempt has been made by classifying the results as no change, improved, greatly improved, and cleared. After six months' treatment two patients were clear apart from slight scarring in

TABLE I.

Case No.	Sex.	Age (years).	Duration of disease (years).	Treatment with chloroquine sulphate.			Treatment with Plaquenil.		
				Max. daily dosage (mg.).	Side effects.	Result.	Max. daily dosage (mg.).	Side effects.	Result.
1	F.	39	13	400	Nausea	Improved	2000	None	Greatly improved.
2	„	37	23	1000	dyspepsia	„	1200	„	„
3	M.	41	8/12	400	Severe eye symptoms	Greatly improved	400	„	„
4	F.	31	5	400	Dyspepsia	Improved	800	„	Cleared.
5	M.	47	20	600	Dyspepsia and eye symptoms	„	400	Dyspepsia	Improved.
6	F.	26	8	600	Dyspepsia	No change	1600	None	„
7	„	42	14	400	Nausea	Improved	800	„	Greatly improved.
8	M.	46	12	600	Dyspepsia and eye symptoms	No change	800	„	Improved.
9	F.	26	5	800	Nausea	Improved	800	„	Greatly improved.
10	„	39	4/12	None	—	—	800	„	Cleared.

one of them (Case No. 4), five were greatly improved and the remaining three showed some improvement. The only side-effect experienced was slight dyspepsia in one patient (Case No. 5). Christiansen (1956) considered that 80% of patients treated with mepacrine or chloroquine relapsed within a period of 12 months after ceasing treatment. It has not yet been possible to assess the relapse rate after Plaquenil treatment.

COMMENT.

It is impossible to draw definite conclusions from so small a series of cases but it seems probable that there is a place for Plaquenil in the treatment of cutaneous lupus erythematosus. It appears to be as effective as chloroquine, tablet for tablet, but is much less liable to cause unpleasant side-effects, thus allowing much higher doses to be given in intractable cases. It has, therefore, some advantages over chloroquine and may even become the drug of choice in the treatment of lupus erythematosus.

SUMMARY.

Ten cases of lupus erythematosus were treated with Plaquenil for six months. Nine had previously been treated with chloroquine but side-effects had occurred. The results suggest that there is a place for Plaquenil in the treatment of cutaneous lupus erythematosus.

My thanks go to Dr. P. F. Borrie for his suggestion to undertake this work and for his help and encouragement during it. I also thank Messrs. Bayer Products Ltd. for supplying the Plaquenil.

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GRANULOMA ANNULARE OF THE SCALP.

STANLEY R. WOOD, M.B., M.R.C.P.

GRANULOMA ANNULARE in the dermis is commonly seen but the subcutaneous type is less well recognized. Since it is unlikely to be diagnosed clinically when it occurs in an unusual situation the following two cases are reported.

CASE REPORTS.

Case 1.—In January 1955 an otherwise healthy boy of three was seen at a surgical clinic with ten or twelve subcutaneous nodules unevenly distributed over the scalp, of three months' duration. The diagnosis of sebaceous cysts was suggested but one was removed and reported as a chronic granuloma. Further nodules developed, and the child was then referred to the Skin Department. A diagnosis of granuloma annulare was made on histology and treatment with vitamin E 200 mg. daily was started. After about six months, during which fresh lesions continued to appear as others subsided, the condition has gradually cleared.

Case 2.—In August 1955 an otherwise healthy boy of two and a half was seen by his doctor with nodules on the scalp of two months' duration which were gradually multiplying. Biopsy suggested granuloma annulare. The nodules continued to appear, and there were about forty present when he was first seen in the Skin Department in January 1956. On vitamin E 200 mg. daily the nodules gradually cleared and had completely gone in twelve months.

In both cases the general health was undisturbed; full blood count, E.S.R. and E.C.G. were normal. Clinically and histologically they were identical. The lesions, varying in size from about 1–2 cm., were cartilaginous, almost bony in consistency, smooth and not tender. They were fixed to the underlying tissues, but the scalp was freely movable over them and of normal appearance. At biopsy the nodules were attached to the galea aponeurotica, encapsulated, with a smooth lustrous surface, and caused slight depression in the outer table of the skull. On the cut surface was a fairly small demarcated, central, moist, lustrous white area surrounded by greyish-red tissue. The histology was that of granuloma annulare (Fig. 1). Rheumatic nodules, with which these lesions could be confused, were excluded by the absence of any systemic disturbance.

COMMENT.

The scalp is mentioned last on the list of involved sites in the latest extensive review of granuloma annulare by Hallewell and Ingram (1935). Graham Little (1908) in his classic monograph mentions two instances of scalp involvement in forty-nine cases, both of which were of dermal type and associated with lesions elsewhere. Subcutaneous lesions on the extremities but not on the

scalp were noted by Jacobi (1931) ; and Grauer (1934) reported a case in some detail in a boy aged two with multiple subcutaneous nodules on the scalp, left wrist and right tibia.

In the two cases here described and observed for more than two years, the scalp has been the only site affected. In both cases the condition remained active for about six months, and during this time nodules were observed to enlarge and subside again over a period of weeks with fresh nodes forming as

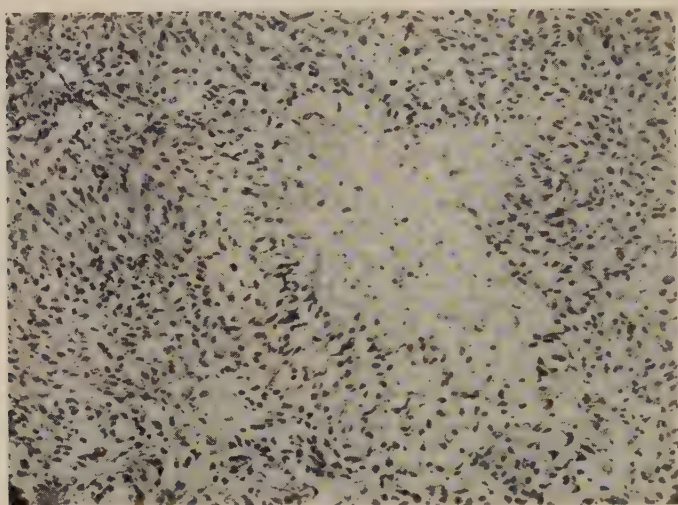


FIG. 1.

others were dying away. This lability contrasts with the relative fixity of the more common dermal type affecting the extremities. It is not possible to assess the part played by vitamin E in the eventual recovery of these two children.

These observations were made during the time I was senior registrar in dermatology to the United Birmingham Hospitals, and I wish to thank Dr. Bernard C. Tate for his permission to publish the cases.

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LICHENOID DERMATITIS DUE TO CHLOROQUINE.

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MOST dermatologists in this country now use chloroquine in preference to mepacrine in the treatment of lupus erythematosus and light sensitivity. Chloroquine does not stain the skin, the results are just as good, if not better, than mepacrine and the toxic symptoms are of less severity, especially the absence of severe lichenoid eruptions.

I have been unable to find in this Journal any mention of lichenoid eruptions due to chloroquine, although three short references were found in the American literature. In the *Year Book of Dermatology* 1954-55 the editors comment that "one of our patients also developed a patchy lichenoid eruption on the extremities due to chloroquine". Goldman *et al.*, (1953) listing the various toxic manifestations of chloroquine, state that "rarely lichenoid dermatitis may occur"; and Alving *et al.*, (1948) in their studies on the toxic manifestations of chloroquine, had two patients who developed lichen planus eruptions after taking 0.5g. chloroquine daily for one year. It is interesting that Samuel Ayres III and Samuel Ayres (Jnr.) treated various dermatoses with chloroquine, including seven patients with lichen planus with "satisfactory results in five".

CASE REPORT.

The patient was a man aged 40 years, working as a miner. For five years he had suffered from a light sensitivity eruption, with many excoriated papules on the face and forearms. He had taken 28 tablets of mepacrine $2\frac{1}{2}$ years previously; the treatment had been discontinued because the result was unsatisfactory.

In March 1957 chloroquine (Nivaquine) was prescribed in a dose of 400 mg. daily, and within a week he was much improved. In July he presented with a lichenoid eruption indistinguishable from that caused by mepacrine. There was a lichenoid dermatitis on the backs of the hands and forearms with papules on the forehead, sides and "V" of neck and pigmented healed lesions on the lumbar area. There was also a generalized lichenoid appearance of the tongue. He complained of a burning sensation on the dorsa of the hands and feet. It is an indication of the great relief obtained in his light sensitivity that he refused to discontinue the tablets, saying his face was "marvellous"; it was only with great difficulty I could persuade him to reduce the dose.

SUMMARY.

The case is reported of a man who developed an extensive lichenoid eruption while taking chloroquine.

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ROYAL SOCIETY OF MEDICINE.

SECTION OF DERMATOLOGY.

President—Dr. LOUIS FORMAN.

16 May 1957.

Pemphigoid with Features of Dystrophic Epidermolysis Bullosa.—Dr. C. H. WHITTLE, Dr. J. A. LEAHY and Dr. R. A. DAVIS.

A woman aged 66.

History.—Blisters first appeared early in 1955 when the patient was in Nairobi. They came first on the loins, later in the mouth and on the neck and new blisters continued to form until treatment produced a partial remission. Previous history and family history negative. When seen on 10.ii.56, there was erythema, with blisters up to 1 cm. diameter, on the wrists, chin, tongue, buttocks, natal fold and posterior aspect of the thighs and legs. Miliun-like epidermal cysts 1–1.5 mm. diameter were present in profusion on the dorsal aspect of the metacarpo-phalangeal joints, the bases of the thumbs, the volar aspects of the wrists and the inner sides of the knees. Some finger and toe nails were shed and others showed severe dystrophy. General condition was good.

Course.—Blister formation ceased or lessened greatly after treatment with arsenic by mouth and the remission continued for five months under daily doses of 0.5–1 g. sulphapyridine. A relapse was treated with dapsone which was effective till she developed jaundice. After three weeks without dapsone, she relapsed and since then blistering has been controlled with prednisone by mouth, 5 mg. *b.d.*

Histology.—The blister is apparently subepidermal and no acantholysis is seen.

Iodine flocculation test + + + +, alpha—2 and gamma globulin increased, blood count normal.

Comment.—The onset in old age and the response to arsenic, sulphapyridine, dapsone and prednisone favour the diagnosis of pemphigoid. The nail dystrophy and epidermal cysts suggest a dystrophic form of epidermolysis bullosa. Such cysts, often seen in epidermolysis bullosa, may occur after vesiculation or blistering from other disorders, such as solar dermatitis (Dietl, 1934), contact dermatitis from flowers (Tolman, 1949) and ? pemphigus (Ormsby, 1933); they may also follow dermabrasion (Epstein and Kligman, 1956). Ormsby's patient showed pemphigoid lesions associated with cysts, the diagnosis between pemphigus and acquired epidermolysis bullosa remaining uncertain. Bloom (1953) described three cases of acquired dystrophic epidermolysis bullosa, with epidermal cysts, which he attributed to sulphonamides. No drugs can be incriminated in our case.

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 EPSTEIN, W. and KLIGMAN, A. M. (1956) *J. invest. Derm.*, **26**, 1.
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Postscript (29.vii.57).—Dr. J. C. Valentine reports no porphyrinuria and no eosinophils in blister fluid.

DISCUSSION.

Dr. G. B. DOWLING : I would strongly support the diagnosis of epidermolysis bullosa. It is characteristic of pemphigoid that after fading, the blisters leave no trace of their former presence. Scars and milium bodies are not seen as they are in this case.

Dr. B. C. TATE : I questioned this patient about treatment and she disagrees entirely about the result ; she does not think it made any difference at all.

THE PRESIDENT : In view of the patient's age, the diagnosis of benign mucous membrane pemphigoid may be suggested. The results of steroid therapy in this disease, in my experience, are disappointing.

Dr. C. H. WHITTLE : I agree that one can be misled by spontaneous remissions but improvement did follow medication, and deterioration occurred when it was stopped.

Dr. BRIAN RUSSELL : The term "senile dermatitis herpetiformis" has sometimes been used as a synonym for pemphigoid, but I have a patient aged 40 with this disease and another aged 79 with the classical middle-age form of dermatitis herpetiformis.

Rodent Ulcer Successfully Treated with Local Injections and Ointment Containing Colcemid.—Dr. N. A. THORNE.

A woman aged 75 had several rodent ulcers treated at another hospital in 1951 with an 8 mg. radium plate applied for 1 hour. I first saw her in June 1956 with a histologically confirmed recurrence of the rodent ulcer at the treated site over the left temple, in the form of a pearly nodule 1.5 cm. in diameter. This was treated by weekly intralesional injections of 1 ml. Colcemid for 14 weeks, plus daily application of 1% Colcemid ointment covered with a small adhesive dressing. After 10 weeks' treatment, the lesion became flat and there was no evidence of the tumour 18 weeks after commencing treatment. The area remains soundly healed 8 months after treatment was completed. Histology showed scarring but no residual carcinoma.

The antimitotic properties of the alkaloid colchicine have been known since 1889 when they were described by Pernice. The alkaloid has an extremely low therapeutic index owing to toxic side effects. Santavy and Reichstein (1950) working in collaboration with Ciba chemists prepared a derivative of colchicine which is 30 times less toxic. It is desacetyl-methyl-colchicine, known also as Colcemid Ciba.

I decided to try the effects of Colcemid by intralesional injection and the local application of 1% Colcemid ointment.

I have so far treated 11 patients, 4 men and 7 women ; in all but one case the basal cell carcinoma was solitary. In 6 patients the lesion had not been treated previously, while the remainder had recurred after radiotherapy. Biopsy was performed before starting treatment in each case. The number of weekly injections required varied from 8 to 14 and the period over which daily ointment was applied ranged from 4 to 10 weeks. Clinical clearance occurred in 5 patients while marked improvement occurred in the remaining 6. The clearance has been confirmed histologically in two cases.

My findings confirm the effectiveness of Colcemid as a method of treating rodent ulcers. I consider that part of the drug's action is by virtue of the acute irritation it sets up in the skin. This probably hinders mitosis of the tumour tissue if it does not in fact destroy the tumour cells.

REFERENCES.

- PERNICE, B. (1889) *Sicilia med.*, **1**, 265.
SANTAVY, F. and REICHSTEIN, T. (1950) *Helv. chim. acta*, **33**, 1606.

DISCUSSION.

Dr. BRIAN RUSSELL : I should like to congratulate Dr. Thorne on his trial of this method. Although rodent ulcers usually respond well to radiotherapy, we should not stop testing other methods. Whenever radiotherapy is contra-indicated, particularly with recurrences, a reliable chemotherapeutic method would be most valuable.

Dr. PETER SMITH : I have treated a dozen cases of common warts with injections of Colcemid once a week for four weeks and in no case was there any change in the warts or any dramatic inflammatory reaction.

Dr. THORNE : I should like to emphasize that as the tumour disappears the inflammatory reaction becomes less marked, rather suggesting that it occurs whether malignant cells are present or not, but that Colcemid has a selective action on cells undergoing rapid mitosis.

Hidradenome Eruptif.—Dr. C. D. CALNAN.

A woman, aged 21.

History.—Two years ago, onset of eruption of small papules, distributed mostly over the flexures. No irritation or other symptoms.

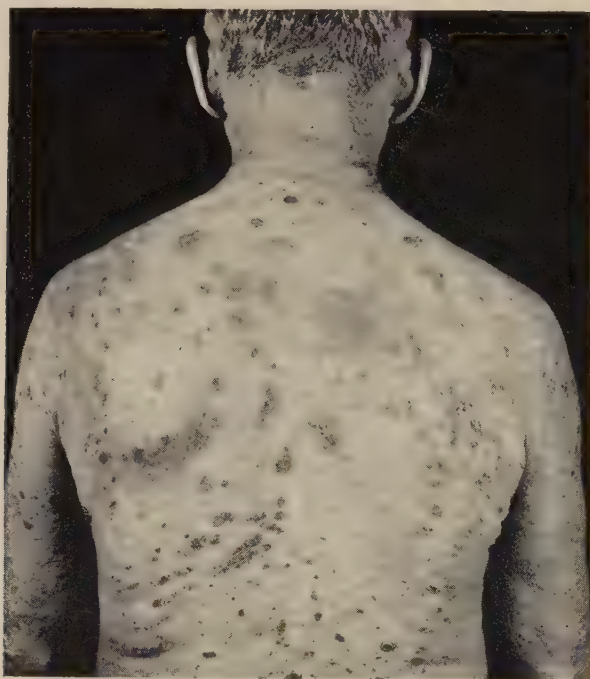
On examination.—There are sparsely scattered flesh-coloured papules in the areas of the elbow flexures, popliteal spaces, inner thighs, pubes, axillae, and the front of the neck. The eyelids are spared.

Histology.—Typical lesions of hidradenome eruptif in the upper cutis.

Comment.—This condition is rare enough to be shown here and I thought the distribution was particularly unusual.

Exudative Discoid and Lichenoid Chronic Dermatitis of Sulzberger and Garbe.—Dr. D. C. G. BETT for Dr. G. C. WELLS.

Jewish man, aged 58. For 18 months this patient has had a widespread eruption which is intensely itchy.



There is a history of eczema in infancy. He also had eczema beginning 21 years ago in Calcutta, which persisted on and off for a period of 11 years.

During the past year he has twice been an in-patient and on both occasions the skin has almost cleared after a few weeks of bland therapy. On the first admission there was widespread exudative dermatitis and some diffuse lichenification and on the second there were more discrete lichenoid plaques (Fig. 1). He usually shows scaly lichenoid lesions about the eyelids and around the mouth and some exudative eczema of the genitalia. A recent exacerbation of his lichenoid eczema was ushered in by urticaria. The morphology of this eruption has varied very markedly from month to month.

General health has been good, but at present this man is anxious and agitated and complains bitterly of irritation. Dr. J. R. A. Madgwick, the psychiatrist who saw him recently, reported that there was no obvious disturbance of mental health apart from mild anxiety and tenseness.

Examination.—The thighs, arms and trunk show numerous discoid lesions of pigmented lichenoid hue, mostly dry but some exudative, and many are surrounded by satellite follicular papules. There is some pigmentation of the buccal mucosa. The finger nails are worn down and highly polished by scratching.

Investigations.—W.B.C., 11,600–20,000. Eosinophils, 12–24%. E.S.R., 20–40 mm./hr. Histology (Dr. H. Haber): "The epidermis shows features of chronic lichenified eczema. In the dermis there is marked perivascular infiltration with round cells, plasma cells and eosinophils."

DISCUSSION.

Dr. G. C. WELLS: These patients are usually disturbed mentally. At some outpatient attendances this man has been extremely agitated and the pruritus has been tremendous. I think that the clinical picture here exactly corresponds with the description of Sulzberger and Garbe (1937) and with my recollection of a case which Dr. M. B. Sulzberger kindly showed me at the New York Postgraduate Hospital in 1948.

Dr. P. J. HARE: I was struck by the clinical similarity to cases of lichenoid drug eruption due to mepacrine or one of the heavy metals. I realize that the peculiar histological picture here is not that of most lichenoid drug eruptions but nevertheless I wonder whether drugs might not be responsible. He is very agitated and agitated people take sedatives.

Dr. G. C. WELLS: I quite agree that this man's present eruption resembles the mepacrine lichenoid dermatosis and we had considered that diagnosis. He last took mepacrine about a year ago and his eruption has been so labile since, that I do not think that mepacrine is a likely cause. I do not know if any other drug would produce this exact picture, but it is an interesting suggestion.

REFERENCE.

SULZBERGER, M. B. and GARBE, W. (1937) *Arch. Derm. Syph., Chicago*, **36**, 247.

The following cases have been published in *Proc. R. Soc. Med.*, **50**, 1019.

Papulonecrotic Tuberculide with Miliary Tuberculosis.—Dr. I. S. HODGSON-JONES.

Incontinentia Pigmenti.—Dr. W. FRAIN-BELL (for Dr. G. C. WELLS).

Necrobiosis Lipidica Diabeticorum and Granuloma Annulare.—Dr. W. FRAIN-BELL.

The following cases also were shown:

Sarcoidosis.—Dr. R. J. CAIRNS.

Prurigo Ferox.—Dr. C. D. CALNAN.

Widespread Naevus with ? Ulerythema Ophryogenes.—Dr. P. R. MONTGOMERY (for Dr. L. FORMAN).

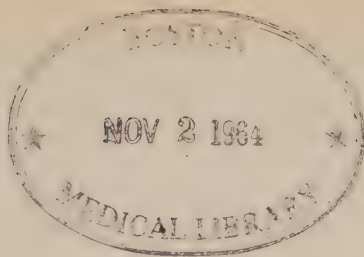
Behçet's Syndrome.—Dr. I. J. MERENLENDER.

OBITUARY.

Professor J. J. Zoon.

Professor Zoon was born in 1902 and died in January of the present year. He was a man of robust physical and mental stature who though harried by illness during much of his working life ranked as a leading figure in dermatology not only in his own country but in the world. Between 1926 and 1957 he published nearly one hundred articles which cover a wide range of dermatological problems. He was invited to U.S.A. as a Rockefeller Foundation Traveller in 1947, and in 1955 he was the foreign guest of honour of the American Academy of Dermatology.

He received his medical education in the University of Utrecht, becoming Chef de Clinique in the Department of Dermatology in 1929 and Professor in 1945. He was engrossed in his department which he organized and conducted in a manner which illuminates his personal outlook and character. He was a master in the traditional art of dermatology and one new disease which he described with meticulous care and accuracy will doubtless bear his name in the future; but he believed especially in the experimental approach and he attracted into his orbit professional scientific workers with whom many of his assistants worked according to their leanings and talents. The output of the Clinic at Utrecht has indeed been considerable and it has always been received in this country with well earned interest and respect. The assistants at Utrecht were deeply attached to their Professor, and their regard was in no small measure shared by the many dermatologists from Great Britain and the Dominions who had the good fortune to know him. Professor Zoon will ever be remembered as an outstanding dermatologist of his era and as a man of simple and endearing character.



XII INTERNATIONAL CONGRESS OF DERMATOLOGY, 1962.

THE following subjects have been provisionally chosen for discussion at the XII International Congress :

1. Malignancies and Tumours of the Skin including Lymphomas. Carcinogenesis and Carcinogens in the Skin.
2. Vascular Disturbances and Their Effects on the Skin.
3. Bio-climatology and the Skin.
4. Psyche and Emotions ; Relationship to Skin Reactions and Diseases.
5. Internal Diseases as Related to Skin and its Diseases.
6. Allergy and Immunology ; Skin Reactions and Diseases.
7. Psoriasis and Arthritis.
8. Geriatric and Paediatric Dermatology.
9. Endocrines and Their Relationship to Cutaneous Disease.
10. Connective Tissue Diseases.
11. The Effect of Radiation and Other Physical Agents on the Skin, including their Genetic Effects.
12. Syphilis and Other Venereal Diseases, including the General Medical and Serological Aspects.
13. Granulomata, including Leprosy, Tuberculosis and Sarcoidosis.
14. Superficial and Deep Fungus Infections, including Public Health and Epidemiological Aspects.
15. The Scalp and Hair ; Embryology, Growth and Diseases.
16. Cutaneous Hazards in Industry ; Their Reduction and Management, including Carcinogens, Poisons, Irritants and Radioactive Agents.
17. Dermatoses due to Animal Parasites.
18. Biochemistry of Skin and Skin Diseases.
19. Anatomy, Pathology and Histopathology of Skin.

Those wishing to suggest further subjects for discussion should communicate with Dr. G. B. Mitchell-Heggs, O.B.E., F.R.C.P., 56 Gower Street, London, W.C.1.

BOOK REVIEWS.

THE FRENCH ATLAS.*

THE fourteenth section of the Atlas is entirely devoted to eczema and contains a considerable amount of text. There are fifteen plates and fifty-seven pages of text. This has perhaps stepped somewhat outside what is usual in an Atlas, but the text not only deals with clinical descriptions and pathology, but reviews the theoretical and experimental work on skin sensitization. These pages dealing with the theoretical aspects of skin sensitivity are very well set out and, by comparison, the account of constitutional factors seems rather bald. Eczema is difficult to photograph but the illustrations in this section are admirable.

The fifteenth section contains one illustration of erythema nodosum (not up to usual standard) and three excellent pictures of Bazin's disease. The largest part of the text is sixty-seven pages on cutaneous tuberculosis, and this section shows how much more than a mere atlas this publication is. The authors deal most competently with all form of cutaneous tuberculosis and the tuberculides together with a very useful summary of treatment. In the diagnosis of tuberculous skin lesions, the reviewer was not able to find mention of the pseudo-tuberculous swimming-bath inoculation which one would think should have received mention; and it is a little surprising that treatment of lupus with calciferol makes so little mention of British authors.

The sixteenth section contains the full text on ichthyosis of various types and on naevi.

The text on ichthyosis includes ichthyosis simplex and the other less common syndromes of harlequin foetus and ichthyosiform erythroderma. These subjects are well covered though it seems strange to encounter the statement that the palms and soles are not affected in ichthyosis simplex and to find no mention of the association of this disease with atopy.

The section on naevi includes a very broad category comprising circumscribed dysplasias of developmental origin. There are thus included the epidermal and dermal naevi, glandular naevi, cutis verticis gyrata, all types of angioma and glomus tumours, lymphangiomas and all pigmentary naevi, both benign and malignant.

In general, these sections fulfil the high standard the authors have already set themselves, but here again a few omissions are a little surprising. No mention could be found of the part played by pregnancy or liver disorders in the production of stellate angiomas, nor of the cardiac failure which may eventually dominate the picture in the Klippel-Trenaunay syndrome.

The plates as always continue to be excellent.

F. R. B.

KAPOSÍ'S SARCOMA.†

DR. BLUEFARB has done us a service by conscientiously abstracting the literature on this peculiar disease, there being a bibliography of 291 references. The approach is somewhat uncritical, and no new light is thrown on the problem.

* *Atlas de Dermatologie*. By P. de Graciansky and S. Boule, Paris: Librairie Maloine S. A. To be issued in 20 parts, price 2000 Francs each. London: H. K. Lewis. Prospectus on request.

† 'Kaposi's Sarcoma. Multiple Idiopathic Hemorrhagic Sarcoma'. S. M. BLUEFARB. Springfield, Illinois: Charles C. Thomas. Pp. 171, 67 illustrations. Price 42s. 0d.

The aetiology is discussed in 25 pages. The disease is much commoner in men, and the incidence is highest between the ages of 50 and 70. The distribution is geographical rather than racial, and 95% of cases are in the labouring class.

Next to the skin, the most frequent sites of involvement are the submucosa of the entire gastro-intestinal tract, the external genitalia, the superficial and deep lymph nodes, the liver and the lungs. Occasionally the cutaneous lesions are late in development and may even be lacking altogether.

There is considerable accord with regard to the histological features, namely infiltrate with numerous spindle-shaped cells; newly-formed capillaries and blood-spaces; haemorrhage; and pigment. Of the spindle-cells, we are told on page 33 that they are believed by most authorities to be of endothelial origin, but on page 68 that most investigators believe that they originate from cells of the connective tissue.

Treatment is unsatisfactory, the most helpful measures being radiotherapy and arsenic.

In each section, the *seriatim* quotation of authorities and individual cases leads to much tiresome repetition.

There are a few errors. On page 54, bottom line, "inability" should surely be "ability". Page 76, line 11, "right labium majora" instead of "majus". Some expressions are unpleasing, e.g. "anatomo-function", page 60, line 18; and "a concentration of cytology", page 132, line 2. There are a fair number of minor textual inaccuracies.

Some of the statements struck the reviewer as very odd. Thus, on page 132: "Although sarcoidosis may simulate Kaposi's sarcoma for a time, this condition presents no infiltrated plaques, vascular elements, visceral lesions of definite predilection". On page 135: "This lesion, of filbert nut size, was flush with the skin surface, and simulated granuloma pyogenicum."

The illustrations are profuse and of fair quality. The photomicrographs would be of more value if the scale were given. The book is well printed and bound.

W. N. G.

CURRENT LITERATURE.

ACQUIRED TOXOPLASMOSIS. D. E. KAYHOE, L. JACOBS, H. K. BEYE and N. B. McCULLOUGH. (1957) *New Engl. J. Med.*, **257**, 1247.

Two patients with toxoplasmosis were given pyrimethamine and sulphonamides with dramatic effect. It is suggested that the drugs suppress rather than cure. Twenty-five mg. pyrimethamine was given daily for 3-4 weeks after a "loading" dose of 50 mg. and 1 g. of triple sulphonamides six-hourly for the same period.

A. D. P.

DIAGNOSIS OF TUBERCULOUS SKIN DISEASES. A. K. DAS. (1956) *Ind. J. Derm.*, **2**, 52.

This is just one short paper (and a good one) in a whole number of this new dermatological journal which is devoted to tuberculosis of the skin. The purpose is educational rather than the breaking of new ground and the standard is high. It is interesting to find in the Editorial that the Calcutta University is creating a Faculty of Dermatology with its professor which will confer a Diploma in Dermatology.

R. D. S.

ACNE VULGARIS AND ITS MANAGEMENT. B. N. BANERJEE. (1957) *Ind. J. Derm.*, **2**, 52.

Vitamin A makes all the difference.

R. D. S.

INCONTINENTIA PIGMENTI. K. D. LAHIRI. (1957) *Ind. J. Derm.*, **2**, 56.

"Imbalance of pituitary-adrenal hormone due to hypervitaminosis A and hypovitaminosis C in the intrauterine life is responsible for incontinentia pigmenti."

R. D. S.

TUBERCULOSIS OF THE SKIN AND ITS RELATION WITH PULMONARY TUBERCULOSIS. B. N. BANERJEE. (1957) *Ind. J. Derm.*, **2**, 69.

About 2.5% of all cases attending a skin clinic in Calcutta have cutaneous tuberculous lesions, mostly lupus, and nearly half of these had pulmonary involvement.

R. D. S.

NICKEL DERMATITIS. K. D. LAHIRI. (1957) *Ind. J. Derm.*, **2**, 110.

This is becoming increasingly common in India. A common after effect is a sharply localized area of leucoderma.

R. D. S.

GRAHAM-LITTLE'S SYNDROME, PSEUDO-PELADE AND LICHEN PLANUS. W. M. STEWART and R. LAUMONIER. (1957) *Ann. Derm. Syph.*, Paris, **84**, 396.

Two cases are reported; in one the pseudo-pelade preceded by ten years the appearance of other lesions; in the other alopecia and follicular hyperkeratoses of the axillae and pubes were followed two years later by an atrophic lichen planus of the scalp. Histologically the first case showed undoubted lichen planus of the hair follicles going on to atrophy. The authors feel these two cases support the assimilation of lichen planus with pseudo-pelade.

F. F. H.

CONSTITUTIONAL VIRILISM. D. FERRIMAN, P. K. THOMAS and A. W. PURDIE. (1957) *Brit. med. J.*, ii, 1410.

An association has been demonstrated between hirsuties and two other masculine characters in women—namely, increased shoulder width and raised 17-ketosteroid excretion. A significant correlation has also been demonstrated between hirsuties and oligomenorrhoea. The condition appears to be genetically determined.

S. T. A.

MELANOSIS CIRCUMSCRIPTA. D. GRINSPAN and J. ABULAFIA. (1956) *Arch. argent. Derm.*, **6**, 351.

The authors describe 10 examples of their own, and review the literature and the newer ideas on the subject. If the lesions become malignant the prognosis is relatively good and the usual extensive extirpation is unnecessary.

G. W. B.

TAR AND THE SKIN. P. D. C. KINMONT. (1957) *Practitioner*, 598, 179.

A purified tar preparation was found to be cosmetically more acceptable than prepared coal tar B.P. Beneficial results were observed in 81% of all patients treated with the synthetic tar, and in 63% with the prepared coal tar B.P.

R. J. C.

THE MANAGEMENT OF THE DRY SKIN. E. J. MOYNAHAN. (1958) *Practitioner*, 135, 180.

Dessication was one of the first problems that animals had to contend with on leaving their aqueous environment. Some animals have been only partially successful in adapting themselves to terrestrial life, moist-skinned animals, such as earthworms and amphibia, being considerably restricted in their habitats. Reptiles, birds and most insects are able to live in drier conditions by virtue of their relatively impermeable outer covering. The survival of the underlying tissues, and ultimately of the organism itself, may depend on the integrity of the epidermis.

The dry skin, whether congenital or acquired, is vulnerable to exogenous influences. It may result from systemic disease, nutritional deficiency or environmental factors. The pliability and resilience of the keratin fibrils in the stratum corneum depend largely upon the degree of hydration of the horny layer.

Treatment is directed towards dealing with any systemic malady or dietary deficiency, of which xeroderma is a manifestation. For local treatment an emollient should be applied to the skin after it has been moistened and excessive exposure to soaps and detergents should be avoided.

R. J. C.

THE MEASUREMENT OF THE CHRONAXY AS A DIFFERENTIAL DIAGNOSTIC AID IN SCLERODERMA-LIKE CONDITIONS. S. JABLONSKA, B. BUBNOW, B. LUKASIAK. (1957) *Derm. Wschr.*, 136, 1201.

The authors have previously shown that the chronaxy is longer in diffuse and circumscribed scleroderma both in the affected and unaffected areas. This method of investigation has now enabled them to differentiate with certainty various scleroderma-like conditions in which clinical and histological distinction is often difficult or impossible.

In lichen sclerosus et atrophicus the chronaxy is normal in unaffected areas. In dermatitis atrophicus sclerodermiformis the chronaxy is normal in unaffected areas and not markedly raised in the thickened areas. In scar-like pseudo-sclerodermatous changes the chronaxy is normal in unaffected areas, and in the same way sclerodactyly can be differentiated from the changes in chronic Raynaud's disease and trophic changes of the skin of the fingers produced by other diseases.

W. G. T.

AN ATTEMPT AT CLARIFYING THE AETIO-PATHOGENIC PROBLEM OF PSORIASIS. L. NARDELLI. (1957) *Derm. Wschr.*, 136, 1235.

The author thinks that the problem of the aetiology of psoriasis is virtually solved. The condition is due to an abnormality of metabolism caused by enzymes. When this abnormality is corrected psoriasis heals. The only question which remains to be answered is the reason for this abnormality which is a hereditary one.

W. G. T.

LICHEN PLANUS PEMPHIGOIDES. T. GRÜNEBERG. (1957) *Derm. Wschr.*, 136, 1238.

A patient suffering from lichen planus was observed for 20 years. Early in this period of observation she developed a widespread bullous eruption which was indistinguishable from pemphigus vulgaris. Complete recovery took place and treatment is not likely to be responsible for this. There has been no recurrence of bullae or vesicles since, though there have been recurrent typical manifestations of lichen planus. Similar cases have been reported by other authors. Cytological studies are of little value in differentiating the condition from true pemphigus vulgaris, but a positive Nikolsky sign is only found in the areas of the vesicles or lichenoid changes, and not in the normal-looking skin.

W. G. T.

THE TREATMENT OF MELANOMA AND ITS PRECURSORS. W. GERTLER and H. GARTMANN. (1957) *Derm. Wschr.*, 136, 1109.

The authors analyse 95 cases of melanoma observed over a period of 10 years. Various forms of treatment have been used—radio-therapy alone, surgery alone and combined methods. There is no clear indication for one or other method of treatment. Decision as to treatment depends on

localization of the tumour, degree of activity and the presence or absence of metastases. The clinical determination of the presence of metastases is not always possible with any degree of certainty. Inguinal glands may be affected long before they become palpable. Very few patients survive after 5 years. Both melanosis circumscripta preblastomatosa and naevus cell naevi must be considered to be potential precursors of malignant melanoma, the former more frequently than the latter. Pigmented moles occurring in later life have an increased tendency to malignancy.

W. G. T.

THE AETIOLOGICAL POSITION OF SUNLIGHT IN SKIN CANCER. H. GARTMANN and E.-M. REINERS. (1957) *Derm. Wschr.*, **136**, 1123.

This is an analysis of 2473 cases of skin cancer. The authors found that epithelioma was commoner in rural male patients than urban ones. Epithelioma of the lower lip was commoner in rural patients and those urban ones more exposed to sunlight, than in town dwellers with indoor occupations. They consider that these types of skin cancer may have to be accepted as occupational diseases. There is no significant difference in basal-celled tumours and in the female. With progressing age it becomes more difficult to decide whether sunlight is responsible or whether the neoplasm is an age manifestation.

W. G. T.

ALLERGIC CONTACT DERMATITIS CAUSED BY WOOD PRESERVATIVES CONTAINING CHROMATES. P. BEHRBOHM. (1957) *Berufsdermatosen*, **5**, 271.

Report of 15 cases of contact dermatitis due to wood preservatives containing chromates, mostly potassium bichromate. The concentration of chromates in the solutions ready for use varied between 1.4% and 4.5% though on a number of occasions dilution was carried out by the workman without accurate measures and higher concentrations were probably employed.

W. G. T.

THE TREATMENT OF ALOPECIA AREATA WITH SYNTHETIC OESTROGEN AND PREDNISONE. C. F. FUNK. (1957) *Derm. Wschr.*, **136**, 1057.

Good results have been observed in the treatment of alopecia areata by subcutaneous injection of diethyl dioxystilbene into the patches and topical application of 0.25% hydrocortisone ointment.

W. G. T.

FOREIGN BODY GRANULOMA DUE TO METALLIC MERCURY. G. HOFF and A. WINKLER. (1957) *Derm. Wschr.* **136**, 1273.

Foreign body granulomata can be caused by a great variety of substances as for instance surgical suture material, talcum powder, silicates, glass wool, beryllium oxide, cactus prickles, dead hair and leather particles from surgical appliances. Whereas lesions of this type were common in the days of topical use of mercurials in the treatment of syphilis, accidental implantation of metallic mercury must be rare. A case is reported in which mercury from a broken thermometer gained entry into the the skin and caused a typical granuloma after 2 months. Toxic manifestations are unlikely in such case on account of the large size of the particle.

W. G. T.

THE SURGICAL TREATMENT OF SEPTIC FOCI IN VARIOUS DERMATOSES. L. GIGLI. (1957) *Arch. ital. Derm. Sif.*, **28**, 421.

A medley of 86 skin patients with septic foci in teeth, tonsils or sinuses were treated in most cases by surgical removal of the focus: 12 of them were "cured" and of these 50% had had an immediate exacerbation of symptoms following the operation, as compared with 28% of those who were not cured.

A. L.

SOME CASES OF ERYSIPELOID TREATED WITH TERRAMYCIN. P. GALIMBERTI. (1957) *Arch. ital. Derm. Sif.*, **28**, 434.

Three active cases responded at once to oral terramycin the total doses being 15, 10 and 6 g. respectively, and there was no subsequent relapse.

A. L.

A CASE OF CHRONIC CIRCUMSCRIBED BENIGN PLASMA-CELLED BALANITIS OF ZOON. R. TAGLIAVINI and M. LANCELOTTI. (1957) *Arch. ital. Derm. Sif.*, **28**, 440.

Said to be a typical example of the disease described by J. J. Zoon (1952) *Dermatologica*, **105**, 1. There was a chronic, indurative, non-suppurative, inflammatory lesion of the glans and

foreskin, that had led to a progressive phimosis, which necessitated partial circumcision. I believe that the diagnosis of balanitis xerotica obliterans would be favoured in Britain. A. L.

IMMUNO-BIOLOGICAL RESEARCHES ON THE COLLAGEN DISEASES WITH PARTICULAR REFERENCE TO LUPUS ERYTHEMATOSUS. I. THE OCCURRENCE IN THE SERUM OF HETEROPHIL HAEMAGGLUTININS. L. RASPOLI. (1957) *Arch. ital. Derm. Sif.*, **28**, 451.

A study of the sera of three groups of patients: (a) normal, (b) collagen diseases, (c) other dermatoses. The author first tested the sera for power to agglutinate the red cells of the ox, horse, guinea-pig, rabbit, pig and sheep. Haemagglutinins were found against all these species but only in the cases of the guinea-pig and rabbit was there any obvious difference between the activity of the collagen disease serum as compared with normal serum. The haemagglutinin titre of normal serum against rabbits and guinea-pigs was always less than 1 in 40. Of collagen disease sera 67% had a haemagglutinin titre greater than 1 in 40 against the rabbit, and 36% against the guinea-pig. The figures for the sera of other dermatoses were 31% and 15% respectively. Cooling the serum increased its activity in some cases, to a maximum of 8 times, and the effect was reversible. Two types of haemagglutinin were detected by absorption of the sera with extracts of ox red cells and guinea-pig kidney. The anti-guinea-pig haemagglutinin was absorbed by both extracts, whereas the anti-rabbit one was unabsorbed by guinea-pig kidney, and mostly absorbed by ox red cells. A. L.

A CONTRIBUTION TO THE KNOWLEDGE OF DYSPROTEINAEMIC CHANGES IN SKIN PATIENTS. M. BONELLI, L. DATOVO and G. ARMUZZI. (1957) *Giorn. ital. Derm.*, **98**, 313.

The plasma proteins were estimated in 352 skin patients and the results have been expressed graphically, disease by disease. The general pattern of each graph is the same: A low albumen/globulin ratio, slight depression of the albumen and elevation of the globulin in the alpha and gamma fractions. The alpha globulins rise in the acute stage and the gamma globulins in the chronic. A. L.

THE COAGULABILITY OF THE BLOOD IN CHRONIC LUPUS ERYTHEMATOSUS. A. LEONI and A. GIOVANNINI. (1957) *Giorn. ital. Derm.*, **98**, 375.

The coagulability of the blood in 20 cases of lupus erythematosus was of a low-normal or sub-normal degree, and the reduction was proportional to the activity of the disease. A. L.

PATHOGENETIC CONSIDERATIONS IN TWO CASES OF PRURIGO NODULARIS OF HYDE. G. PEZZAROSSA. (1957) *Giorn. ital. Derm.*, **98**, 385.

Two elderly women, both asthmatic, one a deaf mute, blinded by cataract, her teeth rotting away, the other incapacitated by chest trouble and subject to chronic abdominal pain. On the grounds of a 6-7% eosinophilia, positive skin reactions to staphylococcal and streptococcal vaccines, a raised E.S.R., and the asthma, the author considers that the disease is primarily an allergic phenomenon which leads to intolerable itching and hence secondary skin changes. A. L.

THE SWEAT RETENTION SYNDROME. L. DATOVO and L. LEVI. (1957) *Giorn. ital. Derm.*, **98**, 403.

An up to date review.

A. L.

CUTANEOUS ADNEXAL TUMOURS: EPITHELIOMA ADENOIDES CYSTICUM, SEBACEOUS EPITHELIOMA, SWEAT GLAND EPITHELIOMA. E. CSERMELY. (1957) *Giorn. ital. Derm.*, **98**, 421.

Five cases contributed material for a histopathological discussion on the origin of these tumours. Epithelioma adenoides cysticum is regarded as naevoid (non-epidermal) in origin as compared with the other two, which are epidermal. Clinically the sweat gland tumours differed from the others in behaving like cancers. A. L.

RADIOTHERAPY OF EPITHELIOMATA OF THE HAIRY SCALP. E. BALZARINI and B. PEROTTI. (1957) *Giorn. ital. Derm.*, **98**, 457.

A review of 48 cases treated over a period of 24 years. The tumours were of slow growth, often large and of long standing, and usually without metastases. Twenty per cent of the tumours had

arisen from multiple sebaceous cysts. Surgical flattening of exuberant growths before radiotherapy was favoured. A surface area greater than 35 sq. cm. precluded cure, but adhesion of the growth to the skull did not necessarily do so. Failure was usually due to insensitivity of the growth, rarely to recurrence. With suitable technique (usually radium mould) complications were not troublesome. Eighteen cases were cured at the first attempt and a further 4 by subsequent treatment.

A. L.

THE POSSIBILITY OF USING A NEW TECHNIQUE FOR CHROMATOGRAPHY IN DERMATOLOGY. S. SACCHI. (1957) *Giorn. ital. Derm.*, **98**, 474.

The method, due to G. Ceriotti (1955) *Nature*, **175**, 897, can deal with dry material. The author has found it handy and accurate.

A. L.

THE ACTION OF HORSE SERUM ON SENSITISED MALIGNANT TISSUE. R. POPOVIĆ, M. PUTNIK and D. ROŠIĆ. (1957) *Voj. San. Pregl. (Beograd)*, **14**, 341.

The authors describe their method of using horse serum in patients with malignant disease (3) and include one with a large papilloma of ear as a control. One patient had a punctate lympho-granulomatosis of skin and enlargement of glands mediastinal and other: one had a spinulocellular carcinoma of the lower lip and adjacent area of skin: the other had an ulcerated cancerous lesion on both sides of the face. The diagnosis was confirmed histologically in all.

To give one example of the method of treatment and the result:

The patient with the two lesions of face received, as did the others, sensitizing subcutaneous injections of the serum beginning with 0.1 c.c. (reaction negative), repeated next day and continued in progressively increasing doses to reach 0.8 c.c. on the tenth day. One lesion received injections in the same dosage, the other injections not higher than 0.1 c.c. The lesion receiving the larger dose involuted very rapidly and in the course of 10 days the skin surface was healed. The other did not respond so well. Three months later the skin was completely normal in the former: in the latter there still remained a remnant of the lesion as on discharge, but quiescent with no sign of further extension.

Photographs show the marked local anaphylactoid reaction that followed treatment of the lip lesion: the rapid reduction of swelling within 14 days, complete within a month and the excellent result when reviewed in 4 months. Photographs show also the rapid improvement in 14 days after injections with serum intracutaneously and into a lymph gland of the patient with lympho-granulomatosis. The histology of the gland injected and neighbouring ones not injected were compared a month after the first injection.

As the papilloma of ear responded like the others to treatment the authors consider that the response to horse serum is non-specific and that other foreign proteins might give a like result.

They point out that this is a unique example of a biological reaction's hindering the evolution of cancer and causing its involution.

There are 12 clinical photographs but not all have reproduced the detail sharply.

There is a summary in English, French and Russian.

M. S. S.

LUPUS ERYTHEMATOSUS EXANTHEMATICUS (LIBMAN-SACHS SYNDROME) AND A STUDY OF 3 CASES. S. TEODORESCU, P. VULCAN, P. DĂNILĂ, G. NICOLAU and M. IVAN. (1956) *Derm. Vener. (Bucharest)* **2**, 99.

In this most interesting up-to-date and comprehensive review of the subject, the authors stress the frequent discrepancy between the skin findings and the gravity of the illness. They allude to the possibility of obtaining the L.E. phenomenon by using urine. There are 8 microphotographs and 2 clinical photographs. Although authorities are mentioned in the text there is no detailed bibliography.

M. S. S.

PSYCHOSOMATIC ASPECTS OF ALLERGY IN CHILDHOOD. H. G. RAFAPORT. (1957) *J. Amer. med. Ass.*, **165**, 812.

Writing as an allergist the author deplores the tendency to overstress the emotional aspects of allergic disorders. "These protracted allergic problems in children are basically immunological, but, during the course of treatment, if these immunological problems are inadequately resolved, then psychological disturbances secondarily intervene and may distort the entire presenting picture."

A. J. R.